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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/896,324	06/29/2001	Bi-Yu Li	TM0011-UT	8386

29748 7590 05/21/2003

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EXAMINER
CHUNDURU, SURYAPRABHA

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 05/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/896,324	Applicant(s) LI ET AL.	
	Examiner Suryaprabha Chunduru	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *14,22 and 23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13 and 15-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's election without traverse of Group I (claims 1-13 and 15-21) in Paper No. 16 is acknowledged.

2. The Information Disclosure Statement (Paper No. 11) filed on April 15, 2002 has been entered and considered.

Priority

3. This instant application claims benefit of a provisional application No. 60/215,596 filed on 6/30/2000.

Non-Statutory Double Patenting

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-10, and 15-21 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 4-6, 8-10, 14, 17, 19-20, 22-24, 26-28, 40-41, 43, 45, 47-48, 50, 52, 54, 55, 57, 59 of copending Application No. 10/055,109 (shi et al.) in view of Goldsbrough (GB 2 295 228).

Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are drawn to a method of amplification and detection of

polynucleotides comprising (a) reverse transcribing an RNA population to obtain a double-stranded cDNA population; (b) digesting said cDNA population with one or more restriction endonucleases having a degenerate recognition or cleavage sequence represented by the formula N^m, where N is the extent of degeneracy, and m is the number of degenerate bases; (c) ligating said restriction fragments to a series (population) of adapters lacking restriction sites, wherein each adapter having a sequence complementary to one of said overhangs; (d) amplifying said restriction fragments. The instant claims further drawn to restriction endonucleases comprising three to eight base cutters, detecting a change in the pattern or amount of RNA expression in a tissue or cell associated with an internal or external factor, and comparing and qunatitating the patterns in said tissue or cells.

The claims of the co-pending application encompass said assay to amplify and detect cDNA polpulation (see page 47, claims 1, 4-6, page 47, claims 8-10, 14, 17, 19-20, 24, 26-28) and a change in pattern or amount of RNA expression (see page 48, claims 40, 41, 43, 45, 47-48, 50, 51, 54, 55, 57, and 59). However, the co-pending claims did not disclose amplification using polymerase chian reaction for no more than 25 cycles.

Goldsbrough teaches a method for identifying and recovering amplified DNA restriction fragments using polymerase chain reaction (see 3, lines 22-24) wherein Goldsbrough discloses that the method comprises detecting polymorphisms (see page 7, lines 14-32); restriction sites comprising degenerate nucleotide sequence (see page 4, lines 3-7); restriction endonucleases comprising 4 to 8 base cutters (see page 4, lines 24-37, page 7, lines12-19).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the method of detecting cDNA polpulations using a method as

claimed by Shi et al. with a PCR amplification method as taught by Goldsbrough to achieve the instant claimed invention as a whole for the expected advantage of developing a PCR based method for obtaining and detecting RNA expression patterns in a biological sample with high sensitivity. Therefore, the instant claims are obvious over Shi et al. in view of Goldsbrough

This is a provisional obviousness-type double patenting rejection.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-13, and 15-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goldsbrough (GB 2 295 228) in view of Warthoe (WO 98/51789).

Goldsbrough teaches a method for selective amplification of restricted DNA fragments using adapter molecules, wherein Goldsbrough discloses that the method comprises (b) cleaving the starting DNA with restriction endonucleases comprising a cleavage sequence or degenerate

recognition site to produce a series of restriction endonuclese digested fragments having a region of overhang (see page 3, lines 11-15, page 11, lines 8-12); (c) ligating said restriction endonuclease fragments to a adaptor molecule having a sequence of bases homologous to subsets of the region of overhang to form a tagged or ligated endonuclease fragment (see page 3, lines 17-20, page 11, lines 14-17); (d) amplifying said ligated restriction fragments using PCR (see page 6, lines 6-13, page 7, lines 25-35, page 11, lines 30-34). Goldbrough also teaches that the method comprises degenerate bases ranging from 1-4 (see page 3, lines 35-36, page 4, lines 23-37, page 5, lines 1-14page 8, lines 1-20): restriction endonucleases comprise 4-6 base cutters (see page 4, lines 7-31); restriction digestion produces overhangs (page 4, lines 14-19); adapters provide priming sites for PCR (see page 6, lines 6-13); detecting PCR products (see page 8, lines 21-33); detecting polymorphisms and changes in nucleotide sequences (see page 6, lines 26-37, page 9, lines 20-30). However, Goldsbrough did not teach reverse transcribing an RNA population to obtain a double-stranded cDNA population.

Warthoe teaches a method for cloning mRNAs (poly A+ RNA) and differential expression patterns of RNA, wherein Watthoe discloses that the method comprises reverse transcribing a mRNA to obtain a double-stranded cDNA fragments (see page 42, lines 5-26, page 43, lines 12-17); digesting cDNA fragments with at least one restriction endonuclease (see page 43, lines 18-20); ligating the fragments with adapter molecules (see page 43, lines 22-24), and amplifying the ligated fragments using primers complementary to an adapter sequence (see page 43, lines 25-31, page 44, lines 1-7); detecting and comparing amounts of RNA expression or patterns (page 51, lines 23-34, page 52, lines 1-16); inserting the PCR products into a vector,

transforming into a suitable host cell to enable the expression of a polypeptide encoding said inserted cDNA fragment (see page 56, lines 13-24).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to combine a method of amplifying restriction fragments as taught by Goldsbrough with the teachings as taught by Warthoe to achieve expected advantage of developing a sensitive and improved method for amplifying cDNA population because Warthoe suggests that "the method provides highly specific reproduction of sequence information which is present in mRNA, even in mRNA which is only present in relatively low amounts and also enables to obtain cDNA fragments derived from a very large percentage of the total number of transcribed genes in relevant cells" (see page 6, lines 23-31) . An ordinary practitioner would have been motivated to combine the teaching of Goldsbrough with the teachings of Warthoe to improve the sensitivity and specificity of the method by including target coding because such inclusion of the limitation would enhance the isolation of new genes and identifying gene expression pattern in any given cell.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 703-305-1004. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's

supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Suryaprabha Chunduru
May 13, 2003

JEFFREY FREDMAN
PRIMARY EXAMINER